## REMARKS

Upon entry of the amendments presented herein, claims 24-30, 32-36, 38-41, 45-51, 53-57, and 62-68 would be pending in the application. Claims 31, 37, 42-44, 52, and 58-61 have been cancelled without prejudice by the present amendment. Applicants seek to amend claims 28-30, 36, 45, 49-51, 53-55, 62, 63, and 68. The specification has been amended to remove hyperlinks and the blank spaces associated with the multiple occurrences of the term "ATCC." These amendments add no new matter.

The paragraph in the specification beginning at page 56, line 5 has been amended to correct an obvious error regarding the position of the CARD domain in the CARD-12 polypeptide. This paragraph has been amended to recite amino acid numbers "1-88" instead of "139-227." Support for the amendment can be found in the specification at, e.g., page 14, line 30, page 16, line 3, page 20, line 16, and page 28, line 2, all of which recite the position of the CARD domain as amino acids "1-88" of SEQ ID NO:2. Accordingly, one skilled in the art would recognize the error in the specification as well as the correction made by the present amendment. These amendments add no new matter.

The minor amendments presented herein would raise no new issues that would require further consideration and/or search. Applicants submit that these amendments would place the claims in condition for allowance or at least present the rejected claims in better form for consideration on appeal, and should therefore be entered after the final rejection under 37 C.F.R. § 1.116.

### Allowable Subject Matter

At page 7 of the Office Action, the Examiner stated that claims 56 and 57 are allowed and that claims 28 and 29 would be allowable if rewritten to overcome the 35 U.S.C. 112, 2nd paragraph rejections and incorporate all of the limitations of the base claim and any intervening claims. Claims 28 has been rewritten as an independent claim and claim 29 has been amended to depend from claim 28.

Objections to the Specification

At page 3 of the Office Action, the Examiner objected to the specification as containing blank spaces after occurrences of "ATCC." The specification has been amended to remove the blank spaces.

At page 3 of the Office Action, the Examiner objected to hyperlinks contained in the specification. The specification has been amended to remove all hyperlinks.

Claim Objections

At page 3 of the Office Action, the Examiner objected to the wording of claim 68. The claim language objected to under this heading has been deleted, thereby obviating the objection.

35 U.S.C. §112, First Paragraph (Written Description)

At pages 3-5 of the Office Action, the Examiner rejected claims 24-27, 30-55, 58-61, and 68 as allegedly failing to comply with the written description requirement. According to the Examiner,

> [t]he specification discloses CARD-12 and its encoding sequences, and although it identifies various domains of the encoded protein, it does not show whether these domains are functional without the rest of the CARD-12 protein. The following meet the written description provisions of 35 USC 112 , first paragraph: SEQ ID NO: 1 (and therefore SEQ ID NO: 3 and sequences encoding SEQ ID NO: 2). The claims are, however, directed to a genus and encompass gene sequences, sequences that hybridize to SEQ ID NO: 3, corresponding sequences from other species, mutated sequences, allelic variants, splice variants, sequences that have a recited degree of identity (similarity, homology), and so forth. None of these sequences meet the written description provision of 35 USC 112, first paragraph. The specification provides insufficient written description to support the genus encompassed by the claim.

Applicants respectfully traverse the rejection in view of the claim amendments and the following remarks. The following sections address the rejections as applied to different groups of claims that are currently pending in the application.

(i) Nucleic Acid Encoding a Polypeptide Containing a Specific Functional Domain of CARD-12

The present application describes the identification and characterization of CARD-12. CARD-12 has a caspase recruitment domain ("CARD"; at about amino acid residues 1-88 of SEQ ID NO:2), a central nucleotide binding site ("NBS") domain (at about amino acid residues 161-323 of SEQ ID NO:2), and a C-terminal leucine rich repeat ("LRR") domain (at about amino acid residues 762-965 of SEQ ID NO:2) (see Table 2 at page 16 of the specification). CARD, NBS, and LRR domains are collectively found in a number of proteins that transmit signals that activate apoptotic and inflammatory pathways in response to stress and other stimuli (see, e.g., specification at page 3, lines 1-3). The CARD domain, which is present in a number of apoptotic signaling molecules, is an effector domain that thought to be involved in homophilic protein-protein interactions, e.g., with downstream CARD-containing signaling molecules (see, e.g., specification at page 4, lines 2-5).

Claims 24-27 are directed to nucleic acids containing a nucleotide sequence that encodes a polypeptide containing amino acid residues 1-88 (CARD), 161-323 (NBS domain), or 762-965 (LRR domain) of the CARD-12 sequence of SEQ ID NO:2.

The precise structural definition of the polypeptides (comprising amino acid residues that correspond to the CARD, NBS domain, or LRR domain of CARD-12) encoded by the nucleic acids of claims 24-27 allows the skilled artisan to readily envision the claimed invention and understand that applicant invented what is claimed. The polypeptides encoded by the nucleic acids of claims 24-27 are described in the specification at, for example, page 8, lines 20-35, and page 20, lines 10-16. Because the polypeptides encoded by the claimed nucleic acids contain a particular functional domain of CARD-12, the polypeptides are expected to necessarily retain the functional activity present in the recited portion of CARD-12. Polypeptides containing such functional regions of CARD-12 can be used, for example, in screening for compounds that modulate a CARD-12 activity associated with that particular region. For a non-limiting example, a polypeptide containing amino acids 161-323 of SEQ ID NO:2 (NBS domain) of CARD-12 is expected to necessarily have nucleotide-binding activity, and can therefore be used to screen for compounds that modulate the ability of CARD-12 to bind to a nucleotide.

In light of the above, applicants submit that the polypeptides encoded by the nucleic acids of claims 24-27 are amply described in the specification, both in terms of structure and associated function, such that the skilled artisan would readily understand applicants to have been in possession of the claimed invention at the time of filing of the present application. Accordingly, applicants request that the Examiner withdraw the rejection.

(ii) Hybridization

Amended claim 45 is drawn to an isolated nucleic acid that contains at least 650 nucleotides and: (a) hybridizes to a nucleic acid consisting of the sequence of SEQ ID NO:3 or the complement thereof under conditions of hybridization at 45°C in 6.0 X SSC followed by washing in 0.2 X SSC, 0.1% SDS at 65°C; and (b) contains a nucleotide sequence that encodes a polypeptide that binds to a caspase or induces apoptosis.

The genus of nucleic acids encompassed by claim 45 does not have substantial variation, since each nucleic acid must encode a polypeptide that has a specified activity (i.e., the ability to bind to a caspase or induce apoptosis) and contain a structurally similar nucleotide sequence (i.e., one that hybridizes under the hybridization and washing conditions recited in the claims). The CARD-12 nucleic acid of SEQ ID NO:3 disclosed in the specification is representative of the claimed genus because: all members of the genus hybridize under high stringency to a CARD-12 nucleic acid; and the skilled artisan can readily perform assays for identifying variants encompassed by the claim having the specified activity. In light of this disclosure, the skilled artisan would have concluded, at the filing of the present application, that applicant was in possession of the necessary common attributes possessed by the members of the genus.

The Examiner cited *Regents of the University of California v. Lilly & Co.*, 119 F.3d 1559 (Fed. Cir. 1997) in support of the present rejection. The discussion in *Lilly* regarding a proper written description for genus claims had to do with a claim drawn to a vertebrate mRNA encoding insulin. The *Lilly* court held that a generic statement, such as the term "mammalian insulin cDNA" is not, without more, an adequate written description of an invention claiming the nucleotide sequence for human insulin. The court's decision in *Lilly* focused on functional claims directed merely to a desired result without structure: "[t]he description requirement of the patent statute requires a description of an invention, not an indication of a result that one might

achieve if one made that invention." *Id.* at 1406. However, the *Lilly* court also took care to indicate that structural information about the claimed genus was different in kind than a mere desired result. The court indicated that in claims involving chemical materials such as proteins and polynucleotides "generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is usually an adequate description of the claimed genus." *Id.*

The present claims are drawn to nucleic acids identified, in part, by their ability to hybridize to a reference polynucleotide sequence under a set of defined hybridization and washing conditions. The ability of a nucleic acid molecule to hybridize to a reference nucleic acid molecule under such defined conditions is dependent on the structure (sequence) of the nucleic acid molecule. Moreover, the claimed nucleic acids are also defined by the recited function of the polypeptide encoded by the nucleotide sequence (i.e., the ability to bind to a caspase or induce apoptosis). The claims are not directed to a desired result without structure, as was the case in *Lilly*. A person of ordinary skill in the art would clearly understand the structural definition of the nucleic acids provided by the claims and would therefore understand applicant to have been in possession of the claimed nucleic acids at the time the application was filed. Accordingly, applicants respectfully submit that the pending "hybridization" claims satisfy the written description requirement.

(iii) Percent Identity

Amended independent claims 30 and 36 are drawn to nucleic acids containing a nucleotide sequence that encodes a polypeptide that: (a) binds to a caspase (claim 30) or induces apoptosis (claim 36); and (b) contains an amino acid sequence that is at least 95% identical to the sequence of SEQ ID NO:2. In addition, independent claim 51 is drawn to a nucleic acid containing a nucleotide sequence that: (a) encodes a polypeptide that binds to a caspase or induces apoptosis; and (b) is at least 95% identical to the sequence of SEQ ID NO:3.

The CARD-12 nucleic acids disclosed in the specification are representative of the claimed genus because: all members of the genus contain or encode a sequence highly similar to a reference sequence (SEQ ID NO:2 or SEQ ID NO:3); and the skilled artisan can readily carry

out assays for identifying variants encompassed by the claim that have the ability to bind to a caspase or induce apoptosis. In light of this disclosure, the skilled artisan would have concluded, at the filing of the present application, that applicants were in possession of the necessary common attributes possessed by the members of the genus.

Similar to the discussion above with respect to the "hybridization" claims, the specification provides relevant identifying characteristics of the claimed nucleic acid molecules. The present claims are drawn to nucleic acids structurally defined by their degree of identity to a reference sequence. The claims thus provide a precise definition of the invention by structure. Moreover, the claimed nucleic acids are also defined by the recited function of the polypeptide encoded by the nucleotide sequence (i.e., the ability to bind to a caspase or induce apoptosis). The claims are not directed to a desired result without structure, as was the case in *Lilly*. A person of ordinary skill in the art would clearly understand the structural definition of the nucleic acids provided by the claims and would therefore understand applicant to have been in possession of the claimed nucleic acids at the time the application was filed. Accordingly, applicants submit that the pending "percent identity" claims satisfy the written description requirement.

35 U.S.C. §112, Second Paragraph (Indefiniteness)

At pages 5-6 of the Office Action, the Examiner rejected claims 62 and 63 as indefinite in their recitation of the phrase "the nucleic acid of claim 23." Claims 62 and 63 have been amended to depend from claim 24. Claims 64-67 were rejected under this heading only because they depend from rejected claims.

In view of these claim amendments, applicants request that the Examiner withdraw the rejection.

35 U.S.C. §102(a) (Anticipation)

At page 6 of the Office Action, the Examiner rejected claims 42-47 as allegedly anticipated by Harzan et al., GenBank™ Accession No. AL121653.

Claims 42-44 have been cancelled, thereby rendering their rejection moot.

Independent claim 45 has been amended to incorporate (in the alternative) the limitations of claims 49 and 50. Because claims 49 and 50 were not rejected under this heading, the incorporation of their limitations into claim 45 is understood to overcome the rejection of claim 45 and claims 46 and 47 that depend therefrom.

In light of these comments and claim amendments, applicants request that the Examiner withdraw the rejection.

## CONCLUSION

Applicants ask that all claims be allowed in view of the amendments and the remarks contained herein.

Please apply any charges or credits to deposit account 06-1050, referencing Attorney Docket No. 07334-136001.

Respectfully submitted,

Date: February 2, 2006

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